Claims

What is claimed is:

1. A human DNase I hyperactive variant.

2. A variant of claim 1 that has DNA-hydrolytic activity that is at least 50% greater than that of native human DNase I as determined in a linear DNA digestion assay.

3. A variant of claim 1 that has DNA-hydrolytic activity that is at least 2-fold greater than that of native human DNase I as determined in a linear DNA digestion assay.

4. A variant of claim 1 comprising an amino acid sequence having at least 90% identity with the amino acid sequence of native human DNase I shown in Figure 1.

5. A variant of claim 1 comprising an amino acid sequence having at least 95% identity with the amino acid sequence of native human DNase I shown in Figure 1.

6. A human DNase I hyperactive variant having an amino acid sequence that differs from the amino acid sequence shown in Figure 1 by the substitution of one amino acid for another at only a single position within the Figure 1 sequence.

7. A variant of claim 6 wherein the amino acid substitution is at one of the following positions within the Figure 1 sequence: Gln9, Glu13, Thr14, His44, Asn74, Ser75, and Thr205.

8. A human DNase I hyperactive variant having an amino acid sequence that differs from the amino acid sequence shown in Figure 1 by the substitution of one amino acid for another at two or more positions within the Figure 1 sequence.

9. A variant of claim 8 wherein at least one of the amino acid substitutions is made at one of the following positions within the Figure 1 sequence: Gln9, Glu13, Thr14, His44, Asn74, Ser75, and Thr205.

10. An isolated nucleic acid encoding a human DNase I hyperactive variant.

11. The nucleic acid of claim 10 comprising a nucleotide sequence that encodes an amino acid sequence having at least 90% identity with the amino acid sequence of native human DNase shown in Figure 1.

12. The nucleic acid of claim 10 comprising a nucleotide sequence that encodes an amino acid sequence having at least 95% identity with the amino acid sequence of native human DNase shown in Figure 1.

13. The nucleic acid of claim 10 comprising a nucleotide sequence that encodes an amino acid sequence that differs from the amino acid sequence shown in Figure 1 by the substitution of one amino acid for another at only a single position within the Figure 1 sequence.

14. The nucleic acid of claim 10 comprising a nucleotide sequence that encodes an amino acid sequence that differs from the amino acid sequence shown in Figure 1 by the substitution of one amino acid for another at two or more positions within the Figure 1 sequence.

15. A method for the treatment of a patient having a pulmonary disease or disorder comprising administering to the patient a therapeutically effective amount of a human DNase I hyperactive variant.

16. The method of claim 15 wherein the disease or disorder is cystic fibrosis.

17. A method for the treatment of a patient having systemic lupus erythematosus comprising administering to the patient a therapeutically effective amount of a human DNase I hyperactive variant.

18. A pharmaceutical composition comprising a human DNase I hyperactive variant and optionally a pharmaceutically acceptable excipient.

19. The composition of claim 18 wherein the composition is in liquid form.

20. The composition of claim 18 wherein the composition is in powder form.